

FIG. 1A

ref. 100

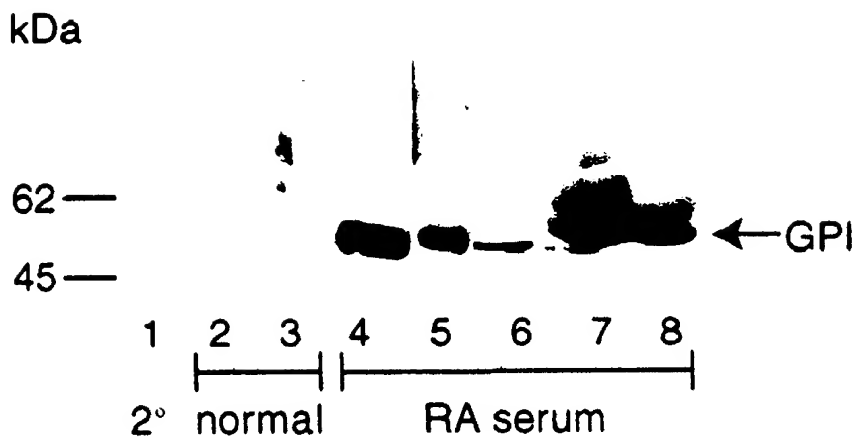


FIG. 1B

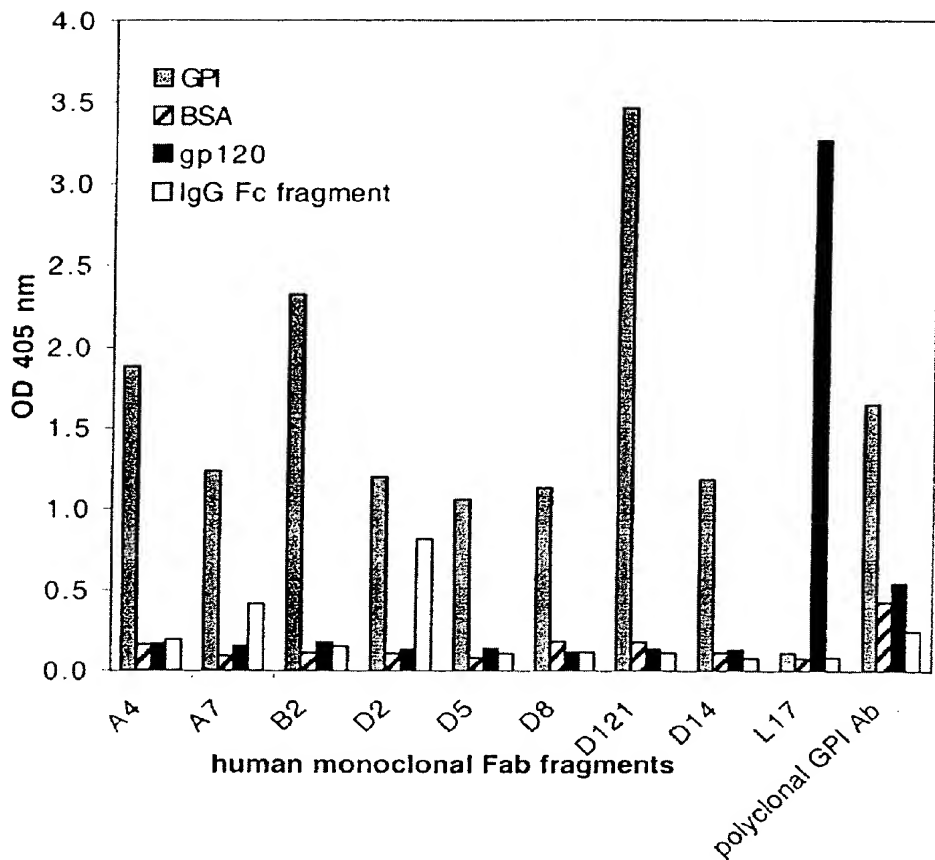


FIG. 2

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
PARTICIPATION IN AUTOIMMUNE DISEASE

INVENTORS NAME: Henrik Ditzel et al.

SERIAL NO.: 09/828,708

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Light Chain Variable AA Sequences

<u>Name</u>	<u>SEQ ID NO.</u>	<u>FR1</u>	<u>CDR1</u>	<u>FR2</u>	
A4	1	PDSLAVSLGERATINC	KSSQSVFYTSNNKNYLA	WYQQKPGQPPKLLIY	
D2	2	PSFLSASVGDRTVITC	RASQGISSYLA	WYQLKPGKAPKLLIY	
D121	3	PGTSLSPGERATLSC	RASQSVSSSYLA	WYQQKPGQAPRLLIY	
B2	4	PDSLAVSLGERATINC	KSSQSVFYTSNNKNYLA	WYQQKPGQPPKLLIY	
D14	5	PGTSLSPGEGATLSC	RASQSVSSSYLA	WYQQRPGQAPRLLIY	
D5	6	PGTSLSPGEGATLSC	RASQSVSSSYLA	WYQQKPGQAPRLLIY	
A7	7	PGTSLSPGERVTLSC	RASQSVSSSYLA	WYQQKPGQAPRLLIY	
<u>Name cont'd</u>		<u>FR3</u>	<u>CDR2</u>	<u>CDR3</u> <u>FR4</u>	
A4	WASTRES	GVPDRFSGSGGTDFLT	TISSLQAEDVAVYYC	QQYYDSYT	FGQGTKLEIKRTVA
D2	AASTLQS	GVPDRFSGSGGTDFLT	TISSLQPEDFATYYC	QQLNSYPLT	FGGGAKEGIRRTVA
D121	GASSRAT	GIPDRFSGSGGTDFLT	TIISRLPEDFAVYYC	QQYGSPPRT	FGQGTKVEIKRTVA
B2	WASTRES	GVPDRFSGSGGTDFLT	TISSLQAEDVAVYYC	QQYYDSYT	FGQGTKLEIKRTVA
D14	GASSRAT	GIPDRFSGSGGTDFST	TISSLQPEDTGTYYC	QQYDNVPTD	FGQGTRELEIKRTVA
D5	GASSRAT	GIPDRFSGSGGTDFLT	TIISRLPEDFAVYYC	QQYGTSP	FGQGTRELEIKRTVA
A7	GASSRAT	GIPDRFSGSGGTDFLT	TIISRLPEDFAVYYC	QQYGSPPRT	FGQGTKVEIKRTVA

FIG. 3AL

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Heavy Chain Variable AA Sequences

Name	SEQ ID NO.	FR1	CDR1	FR2	CDR2	
A4	8	GGGVVQPGRLSLKLSRASGFTFS	SHGSH	WVRQAPGKGLEWVA	LLSDGSKNFYIESVKG	
D2	9AW..LR...V.....	..TM.TM.	
D121	10R.....	.YTF.	VI.Y..NK.Y.AD....	
B2	11	GAEVRKPGTSVRISCRASGNTFT	GHHIH	WVRQAPGQGLQWMG	RINPTGGGVSLAQSFQD	
D14	12	GGGLVQPGGSLRLSCATSGFIEN	SYAMN	WVRQAPGKGLEWVS	RISGNSGSTFYADSVKG	
D5	13	GPGLVRPSQTLTLTCPVSPGSIK	GDSYFWS	WVRQPVGKGLEWIG	RIYGRGTTNYNRVFGS	
A7	14	GAEVKKPGSSVKVSCRASGGTFS	RYAIS	WVRQAPGQGLEWMG	GIIPFPGPVNYAQKFQG	
Name	cont'd	FR3	CDR3	FR4	VH gene	
A4		RFTISKDNKNTLYLQMNSLRIDDTAVYYCAI	SLVGTAFNY	WGQGTTLTVSS	VH3	
D2	R.....LS...PE.....TN	.E..A...D.	VH3	
D121	VE.....	.I.....		VH3	
B2		RVSLTRDRSSNTVFLELSGLTEEDTALYFCAR	PRFNMIREPLDL	WGQGTTLTVSS	VH1	
D14		RFTISRDNKNTAFLRMNSQRAEDTAVYYCAK	DLSSGAYYYGMDV	WGQGTTLTVSS	VH3	
D5		RVSMVSDMSRSQFFLELRDVTAAATAVYYCAR	DKGSEYSYFDP	WGQGIIVNVFVS	VH4	
A7		RVTITADDSTNTAYMGLSSLRSRGDTAVYYCAR	VAYDGGGYNNIPKIYYISYMD	WGKGTTLTVSS	VH1	

FIG. 3AH

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Name	SEQ ID NO:	FR1	CDR1	FR2	CDR2
A4	8	GGGVVQPGRSRLKLSCAASGFTFS	SHGSH	WVRQAPGKGLEWVA	LLSSDGSNKFYIESVKG
D2	9AW..LR...V.....	..TM.		..TM.
D121	10R.....	.YTF.		VI.Y..NK.Y.AD.....
DP-46	R.....	.YAM.		VI.Y.....AD.....
B2	11	GAEVRKPGTTSVRISCRASGNTFT	GHHIH	WVRQAPGQGLQWMG	RINPTGGGVSILAQSFQD
DP-7	K...A..KV..K...Y...	SYMHE...	I...S..ST.Y..K..G
D14	12	GGGLVQPGGSLRLSCATSGFIEN	SYAMN	WVRQAPGKGLEWVS	RISGNSGSTFYADSVKG
VH26	A...T.SS		A...SG...Y.....
D5	13	GFGLVRPSQTLSLTCTPVSPGSIK	GDSYFWS	WVRQPVGKGLEWIG	RIYGRGTTNYNRVFGS
IGHCAK	K.....T..G...S	SG..Y..	.I...A.....	...TS.S....PSLK.
A7	14	GAEVKKPGSSVKVSCRASGGTFS	RYAIS	WVRQAPGQGLEWMG	GIIPPPFGPVNVAQKFQG
VH1-69	K.....	S....I..TA.....

FIG. 3B

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Name cont'd	FR3	CDR3	FR4	VH gene
A4	RFTISKDNSKNTLYLQMNLSIRIDDTAVYYCAI	SLVGTTFAPNY	WGQGTILVTVSS	VH3
D2R.....LS...PE.....TN	.E..A...D.	VH3
D121I.....		VH3
DP-46R.....AE.....R			
B2	RVSLTRDRSSNTVFLELSGLTEEDTALYFCAR	PRFNMIREPLDL	WGQGTIVTVTSS	VH1
DP-7	..TM...T.TS..YM...S.RS....V.Y...			
D14	RFTISRDNKNTAFIRMNSQRAEDTAVYYCAK	DLSSGAYYYIGM	WGQGTIVTVTSS	VH3
VH26LY.Q...L.....	DV		
D5	RVSMVDMRSRQFFLELRDVTAA DTAVYYCAR	DKGSEYSYFDP	WGQGI VVNVFS	VH4
IGHCAK	..TI...T.KN..S.K.SS.....			
A7	RVTITADDSTNTAYMGLSSLRSRSGDTAVYYCAR	VAYDGS GYNNNI	WGKGTIVTVTSS	VH1
VH1-69K..S.....E.....E.....	PKIYYYSYMDV		

FIG. 3B Cont'd

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Clone	Closest Germline	% amino acid homology	% nucleotide homology	R/S ratio FRs	R/S ratio CDRs
A4	DP-46	86	89	6/6:1.0	12/5:2.4
D2	DP-46	87	92	8/6:1.3	4/5:0.8
D121	DP-46	91	95	2/4:0.5	7/0:>7.0
B2	DP-7	67	79	20/17:1.2	<u>14/5:2.8</u>
D14	VH26	87	93	7/3:2.3	5/2:2.5
D5	IGHCAK	73	81	17/16:1.1	13/4:3.3
A7	VH1-69	90	94	7/2:3.5	5/0:>5.0

FIG. 3C

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CDR's Heavy Chain

SEQ ID NO:	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3
15	SHGSH	22	LLSDGSKNFYIESVKG	29	SLVGTAFNY
16	.TM.	23	.IFY.....Y.AD....	30	.E..A...D.
17	.YTF.	24	VI.Y..NK.Y.AD....	31	.I.....
18	GHHIH	25	RINPTGGVSLAQSFQD	32	PRFNMIREPLDL
19	SYAMN	26	RISGNSGSTFYADSVKG	33	DLSSGAYYYGMDV
20	GDSYFWS	27	RIYGRGTTNYNRVFGS	34	DKGSEYSYFDP
21	RYAIS	28	GIIPPFPGPVNYAQKFQG	35	VAYDGSYYNNIPKIYYYSYMDV

CDR's Light Chain

SEQ ID NO:	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3
36	KSSQSVFYTSNNKNYLA	43	WASTRES	50	QQYDYSYT
37	RASQGISSYLA	44	AASTLOS	51	QQLNSYPLT
38	RASQSVSSSYLA	45	GASSRAT	52	QQYGSSPRT
39	KSSQSVFYTSNNKNYLA	46	WASTRES	53	QQYDYSYT
40	RASQSVSSSYLA	47	GASSRAT	54	QQYDNPVDT
41	RASQSVSSSYLA	48	GASSRAT	55	QQYGTSP L
42	RASQSVSSSYLA	49	GASSRAT	56	QQYGSSPRT

FIG. 4A

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Framework Regions, Heavy Chain

SEQ ID	FR1	SEQ ID	FR2
NO:		NO:	
57	GGGVVQPGRSLKLSCAASGFTFS	64	WVRQAPGKGLEWVA
58AW...LR...V.....	64
59R.....	64
60	GAEVKPGTSVRISCRASGNTFT	65	WVRQAPGQGLQWVG
61	GGGLVQPGGSLRLSCATSGFIEN	66	WVRQAPGKGLEWVS
62	GPGLVRPSQTLSLTCTPVSFSGIK	67	WVRQPVGKGLEWIG
63	GAEVKKPGSSVKVSCRASGFTFS	68	WVRQAPGQGLEWVG
SEQ ID	FR3	SEQ ID	FR4
NO:		NO:	
69	RFTISKDNSKNTLYLQMNSLRIDDTAVYYCAI	76	WGQGTLLVTVSS
70R.....LS...PE.....TN	76
71VE.....	76
72	RVSLTRDRSSNTVFLELSGLTEEDTALYFCAR	77	WGQGTIVVTVSS
73	RFTISRDNKNTAFRLMNSQRAEDTAVYYCAK	78	WGQGTIVVTVSS
74	RVSMVDMRSRQFFLELRDVTAAADTAVYYCAR	79	WGQGIIVNVVFS
75	RVITITADDSTNTAYMGLSSLRSRGDTAVYYCAR	80	WGKGTIVTVVSS

FIG. 4B

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
PARTICIPATION IN AUTOIMMUNE DISEASE

INVENTORS NAME: Henrik Ditzel et al.

SERIAL NO.: 09/828,708

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Framework Regions, Light Chain

SEQ ID NO:	FR1	SEQ ID NO:	FR2
81	PDSLAVSLGERATINC	88	WYQQKPGQPPKLLIY
82	PSFLSASVGDRTITIC	89	WYQLKPGKAPKLLIY
83	PGTSLSPGERATLSC	90	WYQQKPGQAPRLIY
84	PDSLAVSLGERATINC	91	WYQQKPGQPPKLLIY
85	PGTSLSPGEGATLSC	92	WYQQRPQGAPRLIY
86	PGTSLSPGEGATLSC	93	WYQQKPGQAPRLIY
87	PGTSLSPGERVTLSC	94	WYQQKPGQAPRLIY
SEQ ID NO:	FR3	SEQ ID NO:	FR4
95	GVPDRFSGSGTDFLTISSLQAEDVAVYYC	102	FGQGTKLEIKRTVA
96	GVPSRFSGSGTEFTLTISSLPEDFAVYYC	103	FGGGAKEVIRRTVA
97	GIPDRFSGSGTDFLTISRLEPEDFAVYYC	104	FGQGTKVEIKRTVA
98	GVPDRFSGSGTDFLTISSLQAEDVAVYYC	105	FGQGTKLEIKRTVA
99	GIPDRFSGSGTDFSTISSLQPEDTGTYYC	106	FGQGRLEIKRTVA
100	GIPDRFSGSGTDFLTISRLEPEDFAVYYC	107	FGQGRLEIKRTVA
101	GIPDRFSGSGTDFLTISRLEPEDFAVYYC	108	FGQGTKVEIKRTVA

FIG. 4B Cont'd

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LIGHT CHAIN NUCLEOTIDE SEQUENCE OF ANTI-GPI ANTIBODIES

A4 - SEQ ID NO:112

CCAGACTCCCTGGCTGTCTCTGGGCGAGAGGGCCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTACACTTCCAAACAATAA
GAACTACTTAGTTGGTACCAGCAGAAACAGGCCAGCCTCTAAGTTGCTCATTTACTGGGCATCCACCCGGGAATCCGGGGTCC
CTGACCGATTACAGTGGCAGCGGTCTGGGACAGATTTCATCTCACCATCAGCAGCCTGCAGGCCTGAAGATGTGGCAGTTATTAC
TGTACGCAATATTATGATTCTGACACTTTTGGCCAGGGGACCAAGCTGGAGATCAACGAACTGTGGCT

D2 - SEQ ID NO:113

CCATCCTTCTCTGCTGCTAGGAGACAGAGTCACCATCACTTTCGGGGCCAGTCAAGGCAATTAGCAGTTATTTAGCCTGGTAT
CAGCTAAACCGGGGAAAGCCCTAAGCTCCTGATCTATGCTGCATCCACTTTGCAAGTGGGTCCCATCAAGGTTTCAGGGCAG
TGGATCTGGGACAGAAITTCATCTCACAAATAAGCAGCCTGCAGCCTGAAGATTTTGCAACTTATTACTGTCAACAGCTTAATAGIT
ACCCTCTCACTTTCGGGGAGGGGCCAAGGTGGGGATCAGACGAACTGTGGCT

D121 - SEQ ID NO:114

CCAGGCACCCCTGCTTTGTCTCCAGGGGAAAGAGCCACCCCTCTCTGCAGGGCCAGTCAGAGTGTTAGCAGCAGTACTTAGCCTG
GTACCAGCAGAAACCTGGCCAGGCTGCCAGGCTCCTCATCTATGCTGCATCCAGCAGGGCCACTGGCATCCAGACAGGTTCAAGTG
GCAGTGGGTCTGGGACAGACTTCACTCTACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTACGACGATATGGT
AG CTCACCTCGGACGTTTCGGCCAAAGGGACCAAGGTGGAAATCAAAACGAACTGTGGCT

B2 - SEQ ID NO:115

CCAGACTCCCTGGCTGTGCTCTGGGGCGAGAGGGCCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTACACTTCCAAACAATAA
GAACTACTTAGTTGGTACCAGCAGAAACAGGCCAGCCTCCTAAGTTGCTCATTTACTGGGCATCCACCCGGGAATCCGGGGTCC
CTGACCGATTACAGTGGCAGCGGTCTGGGACAGATTTCATCTCACCATCAGCAGCCTGCAGGCTGAAGATGTGGCAGTTATTAC
TGTACGCAATATTATGATTCTGACACTTTTGGCCAGGGGACCAAGCTGGAGATCAAACGAACTGTGGCT

FIG. 5A

D14 - SEQ ID NO:116

CCAGGCACCCCTGTCATTGTCACAGGGGAAGAGCCACCCCTCTCTGCAGGGCCAGTCAGAGTGCTTAGCAGCAGCTACCTAGCCTG
GTATCAGCAGAGACCTGGCCAGGCTCCAGGCTCCTCATCTATGTTGCATCCAGCAGGGCCACCGGCATCCCAGACAGATTTCAGTG
GAAGTGGATCTGGGACAGATTTCAGTTTCAACCATCAGCAGCTGTCAGCCTGAAGATACCTGGGACATATTACTGTCAACAAATATGAT
AATGTCCTGACACTTTTGGCCAGGGGACCAAGGCTGGAGATCAACGAACTGTGGCT

D5 - SEQ ID NO:117

CCAGGCACCCCTGCTTTTGTCTCCAGGGGAAGGAGCCACCCCTCTCTGCAGGGCCAGTCAGAGTGTTAGCAGCAGCTACTTAGCCTG
GTACCAAGCAGAAACCTGGCCAGGCTCCAGGGCTCTCATCTATGTTGCATCCAGTAGGGCCACTGGCATCCCAGACAGGTTTCAGTG
GCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGGCAGTGTATTACTGTTCAGCAGTATGGT
ACCTCACCCCTCTTGGCCAGGGACACGACTGGAGATTAAACGAACTGTGGCT

A7 - SEQ ID NO:118

CCAGGCACCCCTGCTTTTGTCTCCAGGGGAAGAGTCACCTCTCTCTGCAGGGCCAGTCAGAGTGTTAGCAGCAGTACTTAGCCTG
GTACCAAGCAGAAACCTGGCCAGGCTCCAGGGCTCCTCATCTATGTTGCATCCAGCAGGGCCACTGGCATCCCAGACAGGTTTCAGTG
GCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGACTTTGCGAGTTTACTGTTCAGCAGTATGGA
AGCTCACCTCGGACGTTGCGCCAGGGACCAAGGTGGAAATCAACGAACTGTGGCT

FIG. 5A Cont'd

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HEAVY CHAIN NUCLEOTIDE SEQUENCE OF ANTI-GPI ANTIBODIES

A4-H - SEQ ID NO:116

GAGCGGTGCTCCAGCCTGGGAGGTCCCTGAAACTCTCCTGTGCAGCCTCTGGATTACATTCAGTAGTCATGGCTCGCACTGGGTC
CGCCAAAGCTCCAGGCAAGGGGCTGGAGTGGGCACTTTGTGCTCTGATGGAAGTAAATAATTCTATATAGAAATCCGTGAAGG
GCCGATTCAACCATCTCCAGGACAATTCTAAGAACACACTGTATCTGCAATGAACAGCCTGAGAAITGACGACACGGGCTGTCTAT
TACTGTGCGAATTCCTGCTGGTGGGAACCTACCGCTTTTAACTACTGGGGCCAGGGAACCCCTGGTCAACCGTCTCCTCA

D2-H - SEQ ID NO:117

GGCGTGTCCAAAGCATGGAGGTCCCTAAGACTCTCTCTGTAGCCTGTGGATTCACTTCAGTAGTCATACCATGCACCTGGGTCCG
CCAGGCTCCAGGCAAGGGGCTGGAGTGGGCACTTATCTATGATGGAAGTAAATAACTATGCAGACTCCGTGAAGGGC
CGATTCAACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAATTGAGCAGCCTAAGACCTGAGGACACGGGCTGTCTATTA
TTGTACGAATTCGAGGTGGGAGCTACCGCTTTTGACTACTGGGGCCAGGGAACCCCTGGTCAACCGTCTCCTCAG

D121-H - SEQ ID NO:118

GGGAGCGGTGCTCCAGCCTGGGAGGTCCCTGAGACTTTCTGTGCAGCCTCTGGATTACCTTCAGTTCCTATACTTTCCACTGG
GTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGCACTTATCATATGATGGAACAAGAAATACTACGCAGACTCCGTGA
AGGCCGATTCAACCATCTCCAGAGACAATTCCAAGAACACTCTATATCTGCAATGAACAGCCTGAGAGTTGAGGACACGGGCTGT
TATTACTGTGCGAATTCATAGTGGAACTACCGCTTTTAACTACTGGGGCCAGGGAACCCCTGGTCAACCGTCTCCTC

FIG. 5B

B2-H - SEQ ID NO:119

GGGGCTGAGGGTGAGGAAGCCCGAACCTCCGIGAGGATCTCTGCAGGGCAJCTGGAAACACUCTTCACTGGCCACCATATTCACTG
GGTCGGCAGAGCCCTGGACAAGGCCCTTCAAGTGGATGGAAAGAAATCAACCCGACTGGCGGGCGGTAGTCTCGCACAGAGTTTC
CAGGACAGAGTCAGCTGACCCAGGACAGGTGCTCCAAATACAGTCTTCTTGGAACTGAGCGGCTCACGGAGGAGGACACGGCCT
TATATTCTGTGCGAGGCCCGGATTAAACAIGATCCGGGAACCTCTTGACCTCTGGGGCCAGGGGACAGTGGTCAACCGTCTCTCTCA

D14-H - SEQ ID NO:120

GGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTCTGTGCAACCTCTGGATTCACTTTAACAGCTATGCCATGAACCTG
GGTCGGCCAGGCTCCAGGGAAGGGCTTGAAGTGGTCTACGTATTAGTGGAAATAGTGGAAAGCACATTTCTACGCAGACTCCGTG
AAGGGCCGGTTCAACCATCTCCAGAGACAATTCCAAAGAACACGGCGTTTCTGCGAATGAACAGCCAGAGCGGAAGACACCGGCCG
TTTATTACTGTGCGAAAGATCTGTGAGTGGTGCATACTACTACGGGATGGACGTCTGGGGCCAAAGGACACGGTCAACCGTC
TCCTCA

D5-H - SEQ ID NO:121

GGCCAGGATTGGTGAGGCCATCACAGACCCTATCCCTCACTGCTCTCCAGGCTCCATTAAAGGTGATAGTTACTTCTG
AGCTGGTCCGTACGCCGTAGGGAAGGACTGGAGTGGATAGGGCGTATCTACGGCAGAGGGACTACCAATTACAAACCGTGT
TCGGGAGTCGAGTCAGTATGTCAGTGGACATGCCAGGAGTCAAGTTTCTTGGAAATTGAGAGATGTGACCCCGCAGACACGGCC
GTCTATTACTGTGCGAGAGACAAGGGGTCCGAATACTCTACTTGTGACCCCTGGGGCCAGGGGAATAGTGGTCAACCGTCTCTCA

FIG. 5B Cont'd

A7-H - SEQ ID NO:122

GGGCTGAGGTGAAGAAGCCTGGGTCCCTCGGTGAAGTCTCCTGCAGGGCTTCTGGAGGCACATTCAGCAGATATGCTA
TCAGCTGGGTGCGACAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAGGGATCATCCCTCCCTTTGGTCCAGTAAACT
ACGCACAGAAGTTCCAGGGCAGAGTCACGATTACCGCGGACGATTCCACGAACACAGCCTACATGGGTCTGAGCAGCC
TGAGATCTGGGGACACGGCCGTGTATTACTGCGGAGAGTGGCCTATGATGGTAGTGGCTATTACAACAATATCCCAA
AGATCTACTACTCTACATGGACGTCCTGGGGCAAAGGGACCAACCGTCACCGTGTCTCCTCAGC

FIG. 5B Cont'd

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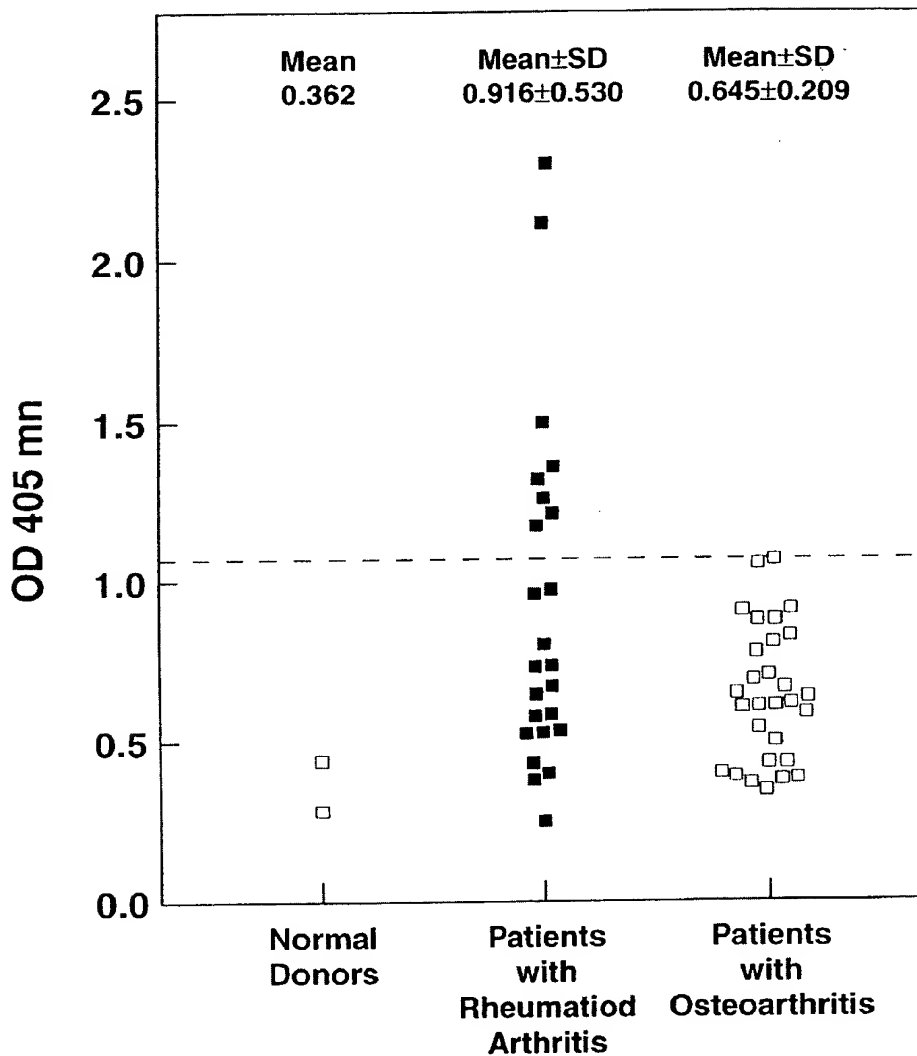


FIG. 6

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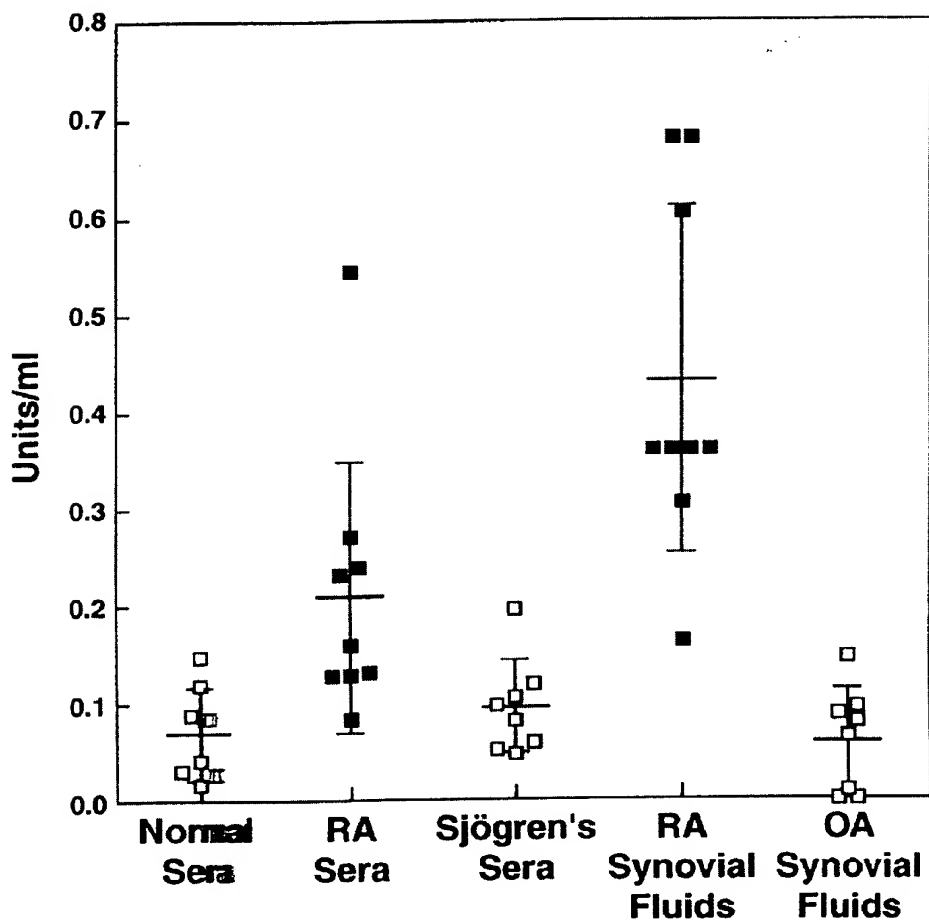


FIG. 7

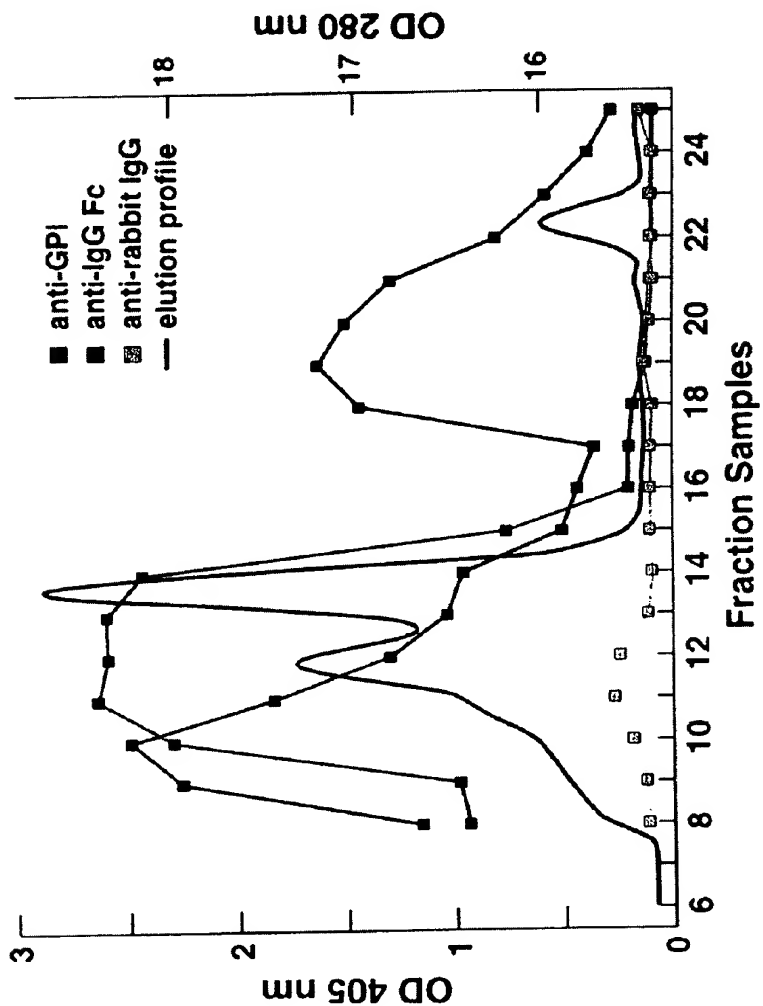


FIG. 8A



FIG. 8B



FIG. 8C

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
PARTICIPATION IN AUTOIMMUNE DISEASE
INVENTORS NAME: Henrik Ditzel et al.
SERIAL NO.: 09/828,708
21/21

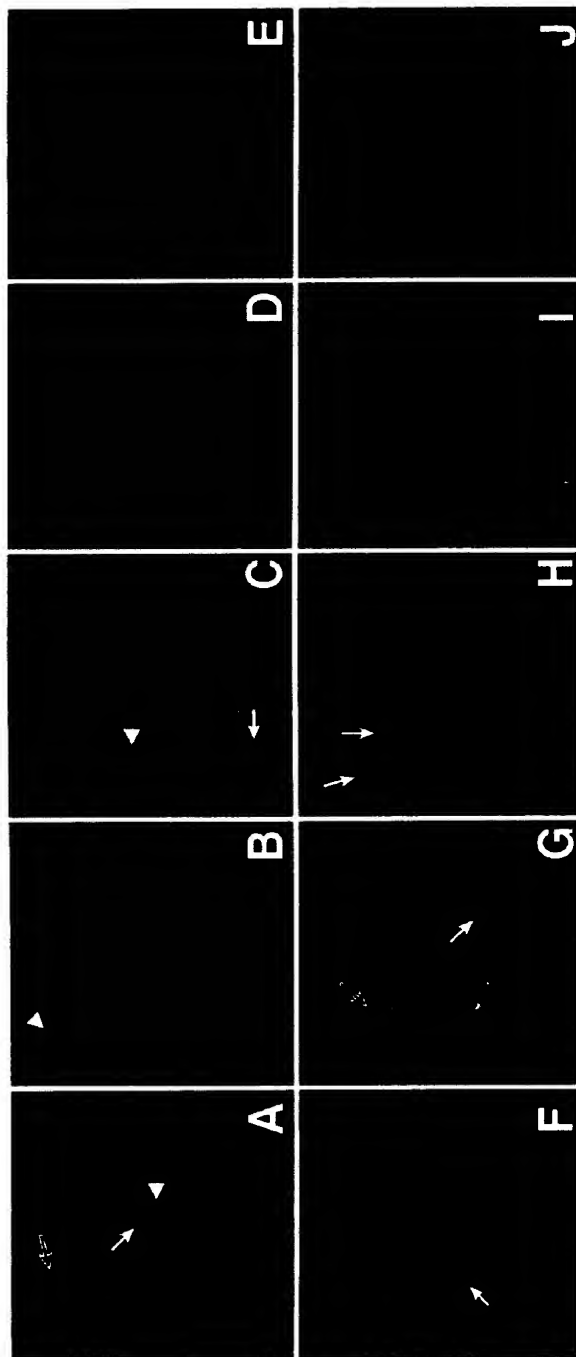


FIG. 9

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